METHODS Myocardial infarction was induced by ligation of the left anterior descending artery in 60 rats. 2 weeks later, animals were randomized to receive of 5×10^6 MSCs labeled with PKH26 in phosphate buffer solution (PBS) (30 rats) or PBS (30 rats) alone injection into the infarction zone in the anterior ventricular free wall. 2, 6 and 12 weeks after MSCs or PBS injection, VFT was measured on infarct zone, infarct marginal zone and non-infarct zone (each period for 10 rats in MSCs group and 10 rats in PBS group). Labeled MSCs were observed in 5μm cryostat sections from each harvested heart.

RESULTS In the MSCs group, there were significant improvements in VFT only on the non-infarct zone compared with the PBS group in short-term period (infarct zone: 3.1±0.9mA vs 3.7±0.9mA $P > 0.05$ infarct marginal zone: 3.0±0.9mA vs 3.6±1.6mA $P > 0.05$ non-infarct zone: 4.9±1.2mA vs 2.3±0.7mA $P < 0.05$). However, in medium-term (infarct zone: 4.2±1.6mA vs 4.0±1.6mA, infarct marginal zone: 2.9±1.9mA vs 2.5±0.8mA, non-infarct zone: 5.1±2.6mA vs 3.4±1.0mA. $P > 0.05$) and long-term period (infarct zone: 3.9±1.3mA vs 4.5±1.7mA, infarct marginal zone: 5.2±2.4mA vs 3.5±1.2mA, non-infarct zone: 5.0±2.0mA vs 3.5±1.4mA. $P > 0.05$), VFT was no improved in the MSCs group. Labeled MSCs were identified on infarct zone and infarct marginal zone, and expressed α-sarcomeric actin and rarely Connexin-43.

CONCLUSIONS The MSCs transplantation only improves the VFT in non-infarct zone in the short-term period. Meanwhile, the MSCs transplantation cannot improve the VFT in medium-term and long-term period. The MSCs differentiated into cardiomyocytes on infarct zone and infarct marginal zone, but expressed rarely Connexin-43.

GW26-e1075

Transplantation of Adipose Derived Stem Cells Improves Cardiac Contractile Function and Electrical Stability in a Rat Myocardial Infarction Model

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OBJECTIVES The purpose of this study was to clarify whether the transplantation of adipose derived stem cells (ADSCs) increases or decreases the incidence of ventricular tachyarrhythmias (VT) in a rat model of myocardial infarction (MI).

METHODS MI was induced experimentally by permanent occlusion of the left anterior descending artery of Lewis rats. ADSCs were harvested from GFP-transgenic rats, and were cultured until passage four. ADSCs (10×10^6) resuspended in 100μL saline or pro-survival cocktail (PSC), which enhances cardiac graft survival, were injected directly into syngeneic rat hearts 1week after MI.

RESULTS The recipients of ADSCs suspended in PSC had a larger graft area compared with those receiving ASDCs suspended in saline at 1 week post-transplantation (number of graft cells/section: 149.8±11.6 vs. 23.4±4.4, $p<0.05$, $n=5$/group). Thereafter, all ADSC recipients were transplanted with ASDCs in PSC. ADSCs were transplanted into infarcted hearts, and the mechanical and electrophysiological functions were assessed. Echocardiography revealed that ADSC recipients had improved contractile function compared with those receiving PSC vehicle (fractional shortening: 21.2±0.8 vs. 15.2±1.3, $p<0.05$, $n\geq12$/group). Four weeks post-transplantation, VT was induced via in vivo programmed electrical stimulation. The recipients of ADSCs showed a significantly lower incidence of induced VT compared with the control (33.2% vs. 84.6%, $p<0.05$, $n\geq12$/group).

CONCLUSIONS ADSCs transplantation decreased conduction velocity and its dispersion in the peri-infarct area. These results suggest that ADSCs transplantation could improve cardiac mechanical and electrophysiological functions in rat after MI.

GW26-e1240

CD226 Molecule Associated with Type 2 Diabetes Mellitus via Modulating Glucose Uptake in Endothelial Cells under Hyperglycemic Conditions

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OBJECTIVES Diabetes mellitus (DM) is one of the most prevalent and serious metabolic diseases. Various complications of type 2 diabetes mellitus (T2DM) are more harmful than T2DM itself, such as two to four times the risk of cardiovascular diseases. CD226 is a co-stimulatory adhesion molecule expressed on immune cells. Signaling cascades involving stimulation of CD226 lead to various biological responses, including immune cell activation and target cell lysis. Thus, CD226 appears to be an integral molecule in immune response in cancer, allergic inflammatory disorders and autoimmune diseases. Recently, emerging evidence supports the role of CD226 in type 1 DM (T1DM), suggesting that it may be involved in the regulation of glucose homeostasis. The aim of the present study was to investigate the effect of CD226 on type 2 DM (T2DM).

METHODS C57BL/6 wild type (WT) and CD226 gene-knockout (KO) mice were fed with high fat diet (HFD) for 14 weeks. We evaluated the possible function of CD226 in glucose metabolism in this HFD-induced diabetic mouse model. Human umbilical vein endothelial cells (HUVECs) were isolated and cultured in endothelial cell growth medium-2 (normal glucose) or added glucose to concentration at 30 mM (high glucose), stimulated with/without palmitate, TNF-α or $CoCl_2$. The change of CD226 expression was examined. In addition, the role of CD226 in glucose uptake in endothelial cells was measured by using D-glucose analog 2-[N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl) mino]-2-deoxy-d-glucose(2-NBDG). The soluble CD226 level in sera from patients with T2DM as well as normal subjects was detected by ELISA.

RESULTS The intraperitoneal glucose tolerance test demonstrated that the CD226 KO mice exhibited improved glucose tolerance. Consistent with this change, high fat feeding evoked markedly compensatory increased islet size in WT mice, but not in CD226 KO mice. RT-PCR results indicated that CD226 was expressed in glucose metabolic tissues and cardiovascular system. Immunohistochemistry staining results further suggested that CD226 was located on endothelial system. In addition, the expression of CD226 was significantly increased in HUVECs cultured in hyperglycemic conditions in the presence of TNF-α compared with that in normal glucose condition. More importantly, knockdown CD226 with human ShRNA lentivirus significantly increased 2-NBDG uptake by 10.6±3.1% in the presence of TNF-α, and the mean fluorescence intensity (MFI) was 112.9±23.1 ($P<0.05$ vs TNF-α group). TNF-α alone decreased the cell glucose uptake compared with the control group by 8.2±3.2%, and the MFI was 45.5±3.9. Furthermore, soluble CD226 in sera from patients with T2DM following oral glucose tolerance test at 1 h, 2 h and 3 h were higher compared with fasting status.

CONCLUSIONS We conclude that low-grade inflammation increased CD226 expression under high glucose state, resulting in decreased glucose uptake in endothelial cells, suggesting that CD226 may play a critical role in glucose metabolism, especially in T2DM.

GW26-e1371

Serum Metabolomics in Acute ST Segment Elevation Myocardial Infarction Patients

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OBJECTIVES To identify the specific metabolic changes by performing the metabolomics analyses on the serum of acute ST-segment elevation myocardial infarction(ASTEMI) patients.

METHODS Ultraperformance liquid chromatography/electrospray ionization quadruple time-of-flight mass spectrometry (UPLC-Q-TOF-MS/MS) and multivariate statistical analysis combined with statistical analysis unit were used to analyze the serum of ASTEMI patients group ($n=15$) in comparison with the healthy control group($n=10$). Further chemiluminescence detection of dehydroepiandrosterone sulfate(DHEAS) was carried out to verify some of the metabolomics findings from the ASTEMI patients.

RESULTS UPLC-Q-TOF-MS/MS revealed that ASTEMI patients and healthy control individuals exhibited distinct metabolomics profiles. Principal component analysis (PCA) and partial least squares discriminant analysis(PLS-DA) demonstrated that ASTEMI patients and healthy control groups were resided in different regions. By using multivariate statistical analysis and statistical analysis, at least nine metabolites were found to markedly differ in the serum of ASTEMI group from those in the healthy individuals. Some differences revealed by the metabolomics study, such as the significant reduction of DHEAS in the serum of ASTEMI patients, were further confirmed by independent chemiluminescence measurements ($P=0.000$).

CONCLUSIONS The unbiased metabolomics analyses reveal that there are significant differences ASTEMI patients and healthy controls on serum metabolite levels. At least nine metabolites in the serum are found to be associated with ASTEMI. These findings may provide new insights regarding the metabolism alterations in ASTEMI patients.